Remarks

Upon entry of the present amendment, independent composition claim 16 would be amended to include composition weight percentages of both the fatty and hydrophilic components. Support for the fatty component can be found on page 4, last line through line 1 of page 4, page 5, lines 18-19 for weight percentage. Support for the hydrophilic component can be found on page 5, lines 1-4, page 6, lines 5-6 and page 6, lines 17-18. Independent process claim would be amended to include elements similar to those of claim 16. Claims 17-26 would be amended to correct certain informalities (*e.g.*, changing "a" to "the" in the preamble).

New claims 29-34 would be added to provide specific protection for preferred compositions. The claims are supported as follows: Claim 29, page 4, last line through line 1 of page 5, page 5, lines 18-19 and page 5, lines 1-4, page 6, lines 5-6 and page 6, lines 17-18; Claim 30, page 5, lines 5-19; Claim 31, page 5, lines 17 and 20-23; Claim 32, page 6, lines 1-4; Claim 33, page 6, line 1; Claim 34, page 5, line 17 and page 6, lines 1 and 2.

Upon entry of this amendment, the status of the claims would be as follows: Claims 16-34 pending; and, claims 1-15 canceled.

The Rejections

I. Rejection of Claims 16-28 Under 35 U.S.C. § 103(a)

Claims 16-28 stand rejected under 35 U.S.C. § 103(a) as unpatentable over Liu et al. ("Liu," U.S. 5,858,986) in combination with Gibson et al. ("Gibson," U.S. 5,811,120). For the reasons set forth below, the rejection is respectfully traversed.

A. Applicants' Invention, Liu and Gibson

As noted in the Background section of Applicants' specification, it is extremely difficult to provide a peroral clarithromycin formulation that affords controlled release of clarithromycin over a twenty-four hour period. Applicants have addressed and solved this problem by providing a formulation in which clarithromycin is mixed in a matrix of a fatty component and a hydrophilic component. That Applicants have afforded a solution is shown in relation to Figures 1 and 2 and in Examples 1 and 3. The examples describe the controlled release of clarithromycin over a twenty-four hour period at pH 3.0 and at pH

6.8, values that represent the pHs of the stomach and duodenum respectively. The materials used in Applicants' formulation are not unique but the combination and result is.

Liu is directed to clarithromycin form I and its synthesis. At column 8, line 46 through column 9, line 11, Liu et al. discusses various excipients and/or carriers. Conventional boiler plate formulation components are noted, but a specific formulation is never disclosed. It accordingly does not disclose peroral release formulations or even remotely suggest how such formulations can be obtained. Furthermore, while Liu reports comparative dissolution tests between clarithromycin crystal form I and form II, the tests have nothing to do with controlled release or the performance of a particular formulation. The only result from the dissolution tests is that form I has an intrinsic rate of dissolution about three times greater than form II.

Gibson is directed to oral pharmaceutical compositions comprising raloxifene in combination with a surfactant, a water soluble diluent, and optionally a hydrophilic binder, a lubricant and disintegrant (Column 2, lines 4-11). Various exemplary formulations are described in the examples provided in Gibson. In making rejections, the Examiner relied on Gibson as disclosing conventional additives in pharmaceutical formulations (*e.g.*, wetting agents; column 3, line 51 to column 4, line 26) and as disclosing the preparation of oral formulations through direct compression.

B. A *Prima Facie* Case of Obviousness Has Not Been Made

Applicants respectfully contend that the Examiner has not made a *prima facie* case of obviousness for the subject claims. Applicants' position is delineated below.

i. Requirements of a *Prima Facie* Case of Obviousness

"The legal concept of *prima facie* obviousness is a procedural tool of examination which applies broadly to all arts. It allocates who has the burden of going forward with the production of evidence in each step of the examination process. The examiner bears the initial burden of factually supporting any *prima facie* conclusion of obviousness." MPEP 2142.

"To establish a prima facie case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the

reference or combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations." MPEP 2143.

a. There Is No Suggestion or Motivation to Combine Liu and Gibson

Pharmaceutical formulations are typically tailored to the specific active ingredient. Clarithromycin and raloxifene differ significantly with respect to structure, activity and chemical stability. The compounds furthermore have different classes of pharmaceutical activities: clarithromycin is an antibiotic; and, raloxifene is an antiestrogen/antiendrogen. One skilled in the art would accordingly not rely on Gibson–a reference solely directed to raloxifene formulations–to modify a clarithromycin formulation.

b. Liu and Gibson Do Not Teach All the Claim Limitations

In an Office Action dated 03/17/2003, the Examiner notes that the inclusion of an adequate weight percentage of the fatty component in Applicants' formulation would explicitly point to its use as a carrier (page 4, lines 1-12). Such use is clearly not contemplated by Liu, according to the Examiner, given that the reference only discusses the use of fatty components as wetting agents (lines 2-4).

Applicants' contend that the amendment of the pending claims is not necessary to confer patentability, but have proposed amendments to expedite prosecution. Upon entry of this amendment, all pending claims will recite a weight percentage range of the fatty component (*i.e.*, 10-36 weight percent) that clearly indicates its use as a carrier rather than a wetting agent.

C. The Rejection of Claims 16-28 Should Be Withdrawn

As a *prima facie* case of obviousness for the subject claims has not been made, Applicants respectfully request that the rejection of claims 16-28 under 35 U.S.C. § 103(a) over Liu in combination with Gibson be withdrawn.

II. Rejection of Claim 19 Under 35 U.S.C. § 103(a)

Claim19 stands rejected under 35 U.S.C. § 103(a) as unpatentable over Liu in combination with Gibson in further view of WO 95/22319. As pointed out above,

Applicants contend that the combination of Liu and Gibson is improper and that the combination, even if permitted, would not provide all the limitations of amended claim 16. Claim 29 cannot be rendered obvious if its parent claim is not. Applicants accordingly respectfully request that the 35 U.S.C. § 103(a) rejection of claim19 be withdrawn.

III. Rejection of Claim 23 Under 35 U.S.C. § 103(a)

Claim23 stands rejected under 35 U.S.C. § 103(a) as unpatentable over Liu in combination with Gibson in further view of Meyer et al. Applicants' argument regarding dependent claim 19 equally applies to claim 23. Applicants accordingly respectfully request that the 35 U.S.C. § 103(a) rejection of claim 23 be withdrawn.

For the reasons set forth above it is believed that entry of the amendment will place this case in condition for allowance. Accordingly, such entry, reconsideration, and allowance are requested. Alternatively, entry is requested as placing the case in better condition for appeal.

Respectfully submitted,

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